

Capillary bio-chip device

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Abstract

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[12] 实用新型专利说明书

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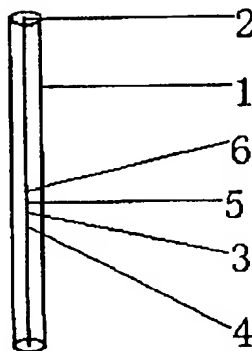
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[54]实用新型名称 毛细管生物芯片装置

[57]摘要

本实用新型涉及一种毛细管生物芯片装置,由内设毛细纤维丝(条)的透明毛细管组成,在毛细纤维丝(条)上点有稳定化的点样物点样线(点)、相应标记物、阳性和阴性对照线(点);利用本装置,一步操作即可对相关的疾病相关基因、病原体、药物或受体、组织或细胞等进行并行检测、识别和鉴定,尤其适合细胞的检测和鉴定,从而得到相关的生命信息。



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权 利 要 求 书

1、一种毛细管生物芯片装置，其特征在于：它是由透明毛细管[1]组成，在该毛细管[1]内设有毛细纤维丝（条）[2]，在毛细纤维丝（条）[2]上点有稳定化的点样物点样线(点)[3]、相应标记物[4]、阳性对照线(点) [5]和阴性对照线(点) [6]。

2、根据权利要求1所述的毛细管生物芯片装置，其特征在于：上述标记物[4]、点样线(点)[3]、阳性对照线(点)[5]和阴性对照线(点) [6]自下而上依次排列，四者之间的距离为0.01—1.0mm，上述四者构成一种检测项目的检测区域。

3、根据权利要求1或2所述的毛细管生物芯片装置，其特征在于：在上述毛细管[1]上设有二种以上的不同检测项目的检测区域，各检测区域的间距为0.1—2.0mm。



说明书

毛细管生物芯片装置

本实用新型属生命科学领域，涉及一种对基因、蛋白质、药物或受体、组织或细胞进行并行检测、识别、鉴定的装置，特别是一种毛细管生物芯片装置。

现有的生物芯片是指包被在固相载体上的高、中、低密度核酸（cDNA、mRNA、PNA）探针、蛋白质（多肽、酶分子、抗原、抗体）、药物或受体、细胞或组织的微点阵（Microarray）。是利用生物大分子间具有特异相互识别的能力而将他们有序的排列在固相载体基片（膜、玻璃片、硅片、瓷片等）上，与待检样品和相应的标记生物分子同时进行特异性反应或杂交，通过自动阅读设备可获得大量有用的生命科学信息。

基因芯片，又称 DNA 芯片，是一种高、中密度的核苷酸（cDNA、mRNA、PNA 探针）微阵列。其制备方法有：其一是采用光蚀刻和原位组合合成化学技术，将大量特定序列的核酸探针有序地固化在载体基片上；其二是将已纯化好的核酸探针利用自动点样设备点样（打印）于载体基片上；其三是利用光诱导技术使基因探针在光导纤维的一端生长；其四是采用分子印章方法多次压印原位定点 DNA 合成于载体基片上；从而构成储存有大量生命信息点阵的基因芯片。

蛋白质芯片又称肽芯片，是将蛋白质（多肽、酶分子、抗原或抗体）固定到固相载体基片上，利用蛋白质分子能特异性与配体分子（抗原或抗体、受体）相结合的原理，然后通过相应的标记分子，用来大规模检测抗原、抗体、受体或酶

分子、多肽片段。其制作方法是将已纯化好的蛋白质分子通过不同的方式点样（打印）于固相载体上；其二是采用光导向多肽合成技术，将具有特定氨基酸序列的多肽链有序地固化在载体基片上。

生物芯片常用的固相载体基片有：有机和无机聚合物薄膜、玻璃片、硅片、瓷片等，该类载体基片通常经过修饰处理，即用各种不同的活化试剂通过化学反应在载体基片表面键合上各种各样的活性基团，以便与点样物种的生物分子共价结合，形成具有不同生物特异性的亲和型载体基片，即生物芯片，用来固定和检测各种不同的活性生物分子，如蛋白质、多肽、酶、核酸、抗原、抗体、药物和受体、组织或细胞等，甚至在载体基片上构建各种各样的微结构（微坑、微沟、微槽、微管、微泵等微型结构或装置），以利于样品的处理和试剂的分配。

上述生物芯片制作工艺复杂，常需要特殊昂贵设备，相应检测手段要求条件高，不利于常规应用。

本实用新型的任务就是提供一种操作简便快速，结果准确可靠，易于观察且制作简便，适合批量生产的毛细管生物芯片装置。

本实用新型的任务是这样完成的：

一种毛细管生物芯片装置，其特征在于：它是由透明毛细管组成，在该毛细管内设有毛细纤维丝（条），在毛细纤维丝（条）上同时固相共价结合多种不同的稳定化点样物的点样线（点）、相应的标记物、阴阳性对照线（点）。

本实用新型采用以上结构后，由于设置了带有毛细纤维丝（条）的毛细管，只需一步操作，即可达到基因、抗原或抗体、药物或受体的并行检测、识别和鉴定的目的，尤其适

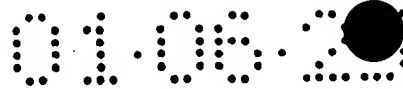
合细胞的检测和鉴定。本实用新型操作简便快速，结果准确可靠，易于观察。适用于疾病相关基因、病原体、药物或受体、组织或细胞等生命科学领域中的检测、识别和鉴定。采用本实用新型，一次吸入待检样品即可并行处理，从而得到相关的生命信息。

附图是本实用新型的一种结构示意图。

下面结合附图对本实用新型作进一步的详细描述。

附图中，1 为毛细管、2 为毛细纤维丝(条)、3 为点样线(点)、4 为标记物、5 为阳性对照线(点)、6 为阴性对照线(点)。

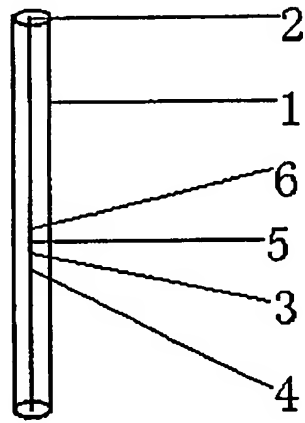
如附图所示，本实用新型毛细管生物芯片装置是由透明毛细管 1 组成，在该毛细管 1 内设有毛细纤维丝（条）2，在毛细纤维丝（条）2 上点有稳定化的点样物点样线(点)3、相应标记物 4、阳性对照线(点) 5 和阴性对照线(点) 6。最外层是透明毛细管 1，用于容纳毛细纤维丝（条）2 和扩展样品。毛细纤维丝（条）2 上含有稳定化的点样物点样线(点)3，点样物可以是 DNA 探针、cDNA 探针、PNA 探针、mRNA、抗原、抗体（包括不同位点的单克隆抗体、抗人 IgM 捕获抗体、抗人 IgG 抗体或二抗抗体）、药物受体、多糖凝集素、细胞或组织等多种生物分子中的任一种或任一组合；两种以上点样物点样线(点)3 自下而上依次平行排列。在毛细纤维丝（条）2 上的相应区域还含有两种以上相应标记物 4，标记物可以是金标记、铁标记、酶标记、荧光标记、化学发光标记、染料标记和放射性标记等标记物中的任一种或任一组合；另外，在毛细纤维丝（条）2 上的相应区域还含有两种以上阳性对照线(点)5 和阴性对照线(点)6。在同一检测项目的检测区域内，自下而上同时含有同一检测项目的相应标记物 4、点样物点样线(点)3、阳性对照线(点)5 和阴性对照线 6，四者之间



有一定的间隙，其距离为 0.01—1.0mm；不同检测项目的检测区域的间距为 0.1—2.0mm，以利于各检测项目间检测区域的分辨和检测；不同检测项目的各检测区域按照自下而上的次序在毛细纤维丝（条）2 上依次等距离排列；检测时可借助透明毛细管的放大作用使显色条带或斑点清晰可辨。

操作时，将该装置的下端插入待检样品中，靠透明毛细管和毛细纤维的毛细现象将样品吸入透明毛细管内，此时待检样品可以沿透明毛细管向上移动并迅速浸渍毛细纤维丝（条），此时待检样品中的待检物同时与点样物和标记物发生特异性反应或杂交，室温 4-60 分钟后观察结果或洗涤后在判读设备上判读结果，以显色条带（点）的有无及多少，判断两种以上待检物的检测、识别和鉴定结果；如在其中一项待检物的检测区域无显色条带（点），则该待检物为阴性，否则为阳性，对于阳性的待检物亦可与其阳性对照线(点)相比较，根据显色条带（点）的颜色深浅而对该待检物进行半定量检测；另外，如果各检测区阳性对照线(点)显色，示该装置有效，否则，示该装置失效。

说明书附图



毛细管生物芯片装置

(Chinese patent publication number 2583395y)

Claims

1, A kind of capillary biochip device, comprises transparent capillary(1) in which there is capillary fibre(thread)(2). There is stable sample line(spot)(3), corresponding marker (4), positive contrast line(5) and negative contrast line(spot)(6) bound on the capillary fibre(2).

2, The device of claim 1, said marker(4), sample line(3), positive contrastline(5) and negative contrast line(6) are arranged orderly from the bottom up. The distances of near two lines of marker(4), sample line(3), positive contrastline(5) and negative contrast line(6) are from 0.01 to 1.0mm and form a region for a testing item.

3, The device of claim 1 or 2, there are over two different regions for testing items on the capillary(1). The distance between two regions is form 0.1 to 2.0mm.

A kind of capillary biochip device

Detailed description

This practical new pattern pertains to life science area, referring to a device, especially a capillary biochip device, used for test, recognition and identification of gene, protein, medicament, tissue or cells.

The present biochip means the high, medial, low densities probe microarray of nucleic acid comprising cDNA, mRNA, PNA and protein (polytide, enzyme molecule, antigen and antibody), medicament, tissue or cells coated on solid support. The mutual biological large molecules are arranged orderly on solid support (glasses, silicon, china) through

the particular specific recognizing abilities, they react or hybridize with samples and corresponding markers simultaneously, then you can get a great deal of useful life science information through auto reading equipment.

Gene chip, also named DNA chip, is a high or medial density probe microarray of nucleic acid(cDNA, mRNA, PNA). Its preparative methods as follows: firstly, using optical etching and in situ synthesis chemical technology, a great deal of nucleic acid probes with specific sequences are solidified orderly on support plate; secondly, the purified nucleic acid probes are spotted (printed) on support plate using auto spotter; thirdly, the gene probe is grown on the end of optical fibre using light-directed technology; finally, the DNA is in situ synthesis on support plate using molecule seal method; the gene arrays are formed which are stored a great deal of useful life information.

Protein chip also named polypeptide biochip, which is made by immobilizing protein (polypeptide, enzyme molecule, antigen and antibody) on solid support, using the principle of protein molecule specific combination with ligand molecule(antibody, antigen and receptor), and using related marker to detect antigen, antibody, receptor, enzyme or polypeptide on a large scale. Its preparative methods as follows: firstly, purified protein molecule is immobilized on the solid support by spotting or printing; secondly, the polypeptide with particular amino acid sequence solidify orderly on the solid plate using light-directed polypeptide synthesis technology.

The usual solid support of biochip comprises: organic and inorganic polymer film, glasses, silicon and china. These supports usually are modified, that is to say, the supports are bound with different active groups using different active reagents through chemical reaction, so the

active groups can be covalent bond with the biological molecules, then form different biological specific affinity solid plate that is biochip, which are used for testing kinds of activated biological molecules such as protein, polytide, enzyme, nucleic acid, antibody and antigen, medicament, receptor, tissues and cells. Some of the solid plate are construct micro structures (micro concave, micro channel, micro trough, micro tube and micro pump), to make for samples processed and agents distribution.

The preparation technics of biochip is very complex and need special expensive equipment. Its means of testing is very rigorous and it is not fit to routine application.

The aim of this practical new pattern is to provide a simple and speedy capillary biochip device in batch, its result is precise and reliable, its result is easily observed and fit for production.

The task of this practical new pattern is accomplished as follows:

A kind of capillary biochip device, comprises transparent capillary(1) in which there is capillary fibre(thread)(2). There is stable sample line(spot)(3), corresponding marker (4), positive contrast line(5) and negative contrast line(spot)(6) bound on the capillary fibre(2).

After adopting said structure of this practical new pattern, the capillary with capillary fibre is used, the aim can be gotten using only one step of test, recognition and identify of gene, antibody, antigen or medicament, especially cells.

The operation of this practical new pattern is simple and speedy, its result is precise and reliable, its result is easily observed. It fits for life science area of diseases related test, recognition and identify including

gene, pathogens, medicament, tissue and cells. When this practical new pattern is used, the indrawn of sample to be tested is only once it can be disposed and related life science information can be gotten.

The enclosed figures are sketch maps of this practical new pattern.

According to the figures, there are further detailed descriptions.

In the enclosed figures: capillary (1), capillary fibre(2), spot line (3), marker (4), positive contrast line (5), negative contrast line (6).

As the figures, the capillary biochip device of this practical new pattern comprises transparent capillary(1) in which there is a capillary fibre(thread)(2). There is stable sample line(spot)(3), corresponding marker (4), positive contrast line(5) and negative contrast line(spot)(6) bound on the capillary fibre(2). The outside is transparent capillary(1), which holds capillary fibre(2) and spreads the sample. Capillary fibre(2) includes stable spotted material line(3). The material is one or their combination of following biological molecules: DNA probe, cDNA probe, PNA probe, mRNA, antigen and antibody (monoclonal antibody with different epitopes, human anti-IgM capture antibody, human anti-IgG antibody and secondary antibody), receptor of medicament, lectin, cells or tissue. When over two dots(3) of samples are parallel arrayed from bottom to top, there are over two related markers(4) on capillary fibre(2). The markers are any one or their combination of gold marker, iron marker, enzyme marker, fluorescence marker, chemiluminescence marker, dyestuff marker and radioactive marker. Moreover, there are also over two positive contrast(5) and negative contrast(6) in capillary fibre(2). In the region for the same testing item, the related markers(4), dots(3), contrast(5) and negative contrast(6) for the same item are arranged from bottom to top, their space is 0.01-1.0mm. The space between the testing regions for different items is

0.1-2.0mm, so good for distinguish different testing regions and test. The testing regions for different items are arrayed in equidistance on capillary fibre(2) form bottom to top. The enlargement of capillary causes the coloration of line or spot more clearly and recognizable.

The underside of said device is insert into the sample, the indrawn sample into transparent capillary by capillarity of the capillary and fibre, the sample can move upwards along transparent capillary vessel and soak capillary fibre rapidly, as the same time, the target in the sample reacts or hybridizes with the material of the dot and the marker. After 4-60 min in room temperature, the result is observed or read by equipment after wash, the result of test is identified according to the coloration line. If there is no coloration line in testing region of one item, the sample is negative, on the contrary, the sample is positive. For positive sample, it can also compare with the positive contrast line for half quantitative test according to the depth of the color of coloration line. Furthermore, if the positive contrast line shows color, the device is available, otherwise the device is unavailable.